

**UNIVERSIDADE NOVA DE LISBOA**

**Faculdade de Ciências Médicas**

**Lisbon, Portugal**



**International Master in Mental**

**Health Policy and Services**

**Coordination : J.M. Caldas de Almeida & B. Saraceno**

**Master's dissertation**

**Report of a Traineeship**

**Audit of antidepressant prescribing in Primary and Mental Health Care: how to address appropriateness and keep a curb on costs. A tool suitable for all contexts?**

**Student: Michele De Francesco**

**Supervisor: Dr. A.Fioritti**

**2013**

## **Acknowledgements**

Many people provided support, information and shared their time with me in developing this dissertation. I feel particularly thankful to Dr. Angelo Fioritti for the guidance in the preparation of this document and for the invaluable moral support. I would like also to thank Professor Jose M Caldas de Almeida, Professor Benedetto Saraceno and Professor Graça Cardoso.

A special thanks goes to Dr. Antonella Piazza for the data management and for providing technical and editing support as for insightful feedbacks.

## **Abstract**

This is the report of a traineeship held in the Local Health Authority of Bologna with the aim to develop skills and competencies in the field of epidemiologically based evaluation oriented projects.

Antidepressants prescriptions have considerably increased all over the world in the last decades. The increasing use of the most expensive agents plays a part in the rising cost of treatments. The Local Health Authority of Bologna has implemented an audit process aimed at improving the appropriateness of outpatient prescriptions focusing on the two branded antidepressants still protected by patent, Escitalopram and Duloxetine.

The Primary Care and the Mental Health Care Departments, as well as the Pharmaceutical Department and the Clinical Governance Unit, were involved in the planning phase of the audit. The audit group, mainly composed of general practitioners and psychiatrists, collected and analyzed scientific evidence on effectiveness and safety of antidepressants. Data on prescriptions of Primary Care Units and Community Mental Health Centers of the Local Health Authority (866.294 inhabitants) were compared, in particular consumption rates of Escitalopram and Duloxetine. The audit group defined the standards to be addressed, the indicators to be evaluated and the actions aimed at reaching the defined goals. NICE guidelines on depression were chosen as reference. The aim of the audit was settled as avoiding Escitalopram and Duloxetine as first choice drugs starting an AD treatment. In order to check the efficacy of the actions undertaken an indicator was selected, consisting in a reduction of 25% of prescriptions of both ADs in outpatient practice and in a 20% reduction of To develop skills and competencies across Primary Care Units.

The pre-audit retrospective report (January-April 2012) showed that outpatient antidepressant treatments were prescribed by GPs in over 90% of cases. Audit actions were implemented between November 2012 and May 2013.

Some relevant actions have been integrated with the audit review, such as small-scale educational meetings with GPs and psychiatrists, outreach visits of the LHA prescribing adviser to GPs and

CMHCs, leaflets for professionals with information extracted from NICE clinical guidelines, implementation of a web consultation service for GPs about evidence on antidepressants.

The feedback report is expected in November 2013 after checking through the standards attained the effectiveness of actions implemented.

A SWOT Analysis was carried out to evidence the strengths and weaknesses, opportunities and threats of the process. As identification of weaknesses may be useful to identify relevant strategies for internal improvement, so the knowledge of threats can amortize factors that may have adverse impacts beyond the control of the Mental Health Department. Better understanding of the strengths and the opportunities facilitates the achievement of the goals set in the project.

The first and not least upshot of this process has consisted in further integration between Primary and Mental Health Care, thus enabling the LHA to put the change into practice.

**Key words:** *SWOT analysis, audit, antidepressants, appropriateness, drug utilization, cost evaluation, primary care.*

## Resumo

Este é o relatório de um estágio realizado na Autoridade de Saúde Local de Bolonha com o objectivo de desenvolver capacidades e competências na área de projectos orientados para a avaliação com base epidemiológica.

As prescrições de anti-depressivos aumentaram consideravelmente em todo o mundo durante as últimas décadas. O uso cada vez maior dos agentes mais dispendiosos desempenha um papel na subida do custo dos tratamentos. A Autoridade de Saúde Local de Bolonha implementou um processo de auditoria com o objectivo de melhorar a adequação das prescrições de pacientes externos, centrando-se em dois anti-depressivos de marca ainda protegidos por patente, Escitalopram e Duloxetine.

Os Departamentos de Cuidados de Saúde Primários e de Cuidados de Saúde Mental, assim como o Departamento Farmacêutico e a Unidade de Gestão Clínica, estiveram envolvidos na fase de planeamento da auditoria. O grupo da auditoria, maioritariamente composto por médicos de clínica geral e psiquiatras, reuniu e analisou provas da eficácia e segurança dos anti-depressivos. Os dados sobre as prescrições das Unidades de Cuidados de Saúde Primários e dos Centros de Saúde Mental Comunitários da Autoridade de Saúde Local (866.294 habitantes) foram comparados, em particular as taxas de consumo de Escitalopram e Duloxetine. O grupo da auditoria definiu os standards a serem abordados, os indicadores a serem avaliados e as medidas a empreender para atingir os objectivos definidos. As directrizes do NICE sobre a depressão foram escolhidas como referência. O objectivo da auditoria foi definido como evitar o Escitalopram e Duloxetine como medicamentos de primeira escolha num tratamento anti-depressivo. De modo a verificar a eficácia das medidas empreendidas foi seleccionado um indicador, consistindo numa redução de 25% das prescrições de ambos os anti-depressivos na prática clínica de pacientes externos e numa redução de 20% da variabilidade nas Unidades de Cuidados de Saúde Primários.

O relatório retrospectivo pré-auditoria (Janeiro a Abril de 2012) revelou que os tratamentos com anti-depressivos para pacientes externos eram prescritos pelos médicos de clínica geral em mais de

90% dos casos. As medidas da auditoria foram implementadas entre Novembro de 2012 e Maio de 2013.

Algumas medidas relevantes foram integradas com a revisão da auditoria, tais como reuniões educacionais de pequena escala com os médicos de clínica geral e psiquiatras, visitas de apoio do assessor de prescrições da Autoridade de Saúde Local aos médicos de clínica geral e Centros de Saúde Mental Comunitários, panfletos para profissionais com informação retirada das directrizes clínicas do NICE, implementação de um serviço de consulta na Web para médicos de clínica geral sobre provas relativas a anti-depressivos.

O relatório de feedback é aguardado em Novembro de 2013 depois de se verificar nos standards atingidos a eficácia das medidas implementadas.

Foi realizada uma análise SWOT para comprovar as forças e fraquezas, as oportunidades e ameaças do processo. Como identificação de fraquezas poderá ser útil identificar estratégias relevantes para melhoria interna, para que o conhecimento das ameaças possa amortizar factores que possam ter impactos adversos que fujam ao controlo do Departamento de Saúde Mental. Uma melhor compreensão das forças e das oportunidades facilita a consecução dos objectivos estabelecidos no projecto.

O primeiro, mas não o último, resultado deste processo consistiu numa maior integração entre os Cuidados de Saúde Primários e de Saúde Mental, permitindo assim que a Autoridade de Saúde Local coloque as alterações em prática.

**Palavras-chave:** *análise SWOT, auditoria, anti-depressivos, adequação, utilização de medicamentos, avaliação de custo, cuidados primários.*

## Resumen

El presente documento es el informe de un periodo de prácticas llevado a cabo por las autoridades sanitarias locales de Bolonia con el objetivo de desarrollar destrezas y competencias en el campo de proyectos de evaluación con base epidemiológica.

La prescripción de antidepresivos ha aumentado considerablemente en todo el mundo durante las últimas décadas. El uso cada vez mayor de los agentes más caros ha supuesto un aumento de los costes de los tratamientos. Las autoridades sanitarias locales de Bolonia han implementado un proceso de auditoría con el objetivo de mejorar la idoneidad de las prescripciones ambulatorias, centrándose en los dos antidepresivos de marca que aún están protegidos por patentes: Escitalopram y Duloxetina.

Los departamentos de atención primaria y de salud mental, así como el departamento de farmacia y la unidad de dirección clínica, nos implicamos en la fase de planificación de la auditoría. El grupo de auditoría, compuesto principalmente por médicos generalistas y psiquiatras, recopiló y analizó evidencias científicas acerca de la eficacia y seguridad de los antidepresivos. Se compararon los datos relativos a las prescripciones de las unidades de atención primaria y de los centros comunitarios de salud mental controlados por las autoridades sanitarias locales (866.294 habitantes), más concretamente, los niveles de consumo de Escitalopram y Duloxetina. El grupo de auditoría definió los estándares que debían valorarse, los indicadores que debían evaluarse y las acciones necesarias para alcanzar los objetivos definidos. Como referencia, se eligieron las directrices NICE sobre depresión. Se estableció como objetivo de la auditoría la eliminación del Escitalopram y de la Duloxetina como fármacos de primera opción al inicio de un tratamiento con antidepresivos. Para comprobar la eficacia de las acciones llevadas a cabo, se seleccionó un indicador que establecía una reducción del 25% de las prescripciones de ambos antidepresivos en la práctica ambulatoria y una reducción del 20% en los niveles de variabilidad para el desarrollo de destrezas y competencias en las diferentes unidades de atención primaria.

El informe retrospectivo previo a la auditoría (enero-abril 2012) mostró que los médicos generalistas prescribían tratamientos antidepresivos a los pacientes del sistema ambulatorio en más del 90% de los casos. Las acciones de la auditoría se implementaron durante el periodo comprendido entre noviembre de 2012 y mayo de 2013.

Con la evaluación de auditoría, se pusieron en marcha diferentes acciones relevantes, como

reuniones educativas con grupos reducidos de médicos generalistas y psiquiatras, visitas divulgativas de los asesores de prescripciones de las autoridades sanitarias locales a médicos generalistas y centros comunitarios de salud mental, reparto de folletos para profesionales con información extraída de las directrices clínicas NICE, o la implementación de un servicio de consultas a través de Internet para médicos generalistas acerca de las evidencias científicas relativas a los antidepresivos.

Se espera contar con el informe de evaluación en noviembre de 2013, después de comprobar la eficacia de las acciones implementadas en relación con los estándares establecidos.

Se llevó a cabo un análisis DAFO para dar cuenta de las debilidades, las amenazas, las fortalezas y las oportunidades del proceso. Al igual que la identificación de las debilidades puede resultar útil con el objetivo de identificar estrategias relevantes para obtener una mejora interna, el conocimiento de las amenazas permite amortizar aquellos factores que pueden suponer un impacto negativo más allá del control del departamento de salud mental. Un mayor conocimiento de las fortalezas y oportunidades facilitará la consecución de los objetivos establecidos en el proyecto.

La primera consecuencia importante de este proceso ha sido una mayor integración entre las unidades de atención primaria y de salud mental, lo que ha permitido a las autoridades sanitarias locales poner en práctica los cambios previstos.

**Palabras clave:** *análisis DAFO, auditoría, antidepresivos, idoneidad, uso de fármacos, evaluación de costes, atención primaria.*



<b>Contents</b>	<b>Pages No</b>
<b>Foreword</b>	<b>10</b>
<b>Introduction</b>	<b>12</b>
<b>Antidepressant Prescribing</b>	<b>17</b>
<b>Aims of the audit: addressing appropriateness and reducing costs</b>	<b>22</b>
<b>Methods, Setting and Data Sources</b>	<b>24</b>
<b>The Audit Process</b>	<b>35</b>
<b>Discussion</b>	<b>39</b>
<b>SWOT Analysis</b>	<b>44</b>
<b>Conclusion</b>	<b>45</b>
<b>References</b>	<b>47</b>

## Foreword

The present study has been thought on the basis of local needs that have arisen in the context of Bolzano, and in particular the need of evaluating the appropriateness of antidepressant prescribing and costs. For this purpose I took contact with my supervisor, Dr. Angelo Fioritti, who was leading this project in Bologna, and I started to attend the psychiatric department of Bologna to see how the project worked.

As I've tried to carry out the project in Bolzano I met serious problems of data access and coordination of the work: I found that the data base of the Pharmaceutical Department could not communicate with that one of the Mental Health Department and also important data were largely incomplete or missing. Although in the initiation phase of the study the people involved have always been willing to cooperate, the attempt to introduce a research model clashed with the routine work and has led to the abandonment of the project.

Ultimately the reasons for the failure of the initial project planned in Bolzano can be listed in the following points:

- an insufficient proper assessment of the context and the financial and material resources
- overestimation of personal resources like skills, knowledge and motivation of the involved persons
- lack of a collaborative network

Theoretical development and practical experience are continually producing new insights. The failure of the project in Bolzano was a lesson on how a good project management has to be built taking into account strengths and weaknesses.

The study could not be conducted in Bolzano for the problems listed above.

It's important to learn from failures and given the importance of the project I did not want to abandon completely the original research project. My tutor, Angelo Fioritti, and I agreed that my thesis work could be positioned inside the Bologna project. In this way I was able to follow the genesis of the project within all the steps, from the planning phase to the construction and coordination of collaborative groups to the data analysis and data return.

It was therefore decided that my thesis would consist in a traineeship report held in Bologna.

The traineeship started in autumn 2012 and ended in summer 2013. During this time I went to Bologna when meetings took place.

In the planning phase meetings between the Direction of the Mental Health Department, the Pharmaceutical Department, the Clinical Governance Unit and the Primary Care Department took place on september 24<sup>th</sup> and october 8<sup>th</sup>.

The 20<sup>th</sup> of february I participated to an educational meeting with GPs.

During the spring I met Ms. A. Piazza for the data analysis meetings on 15<sup>th</sup> and 29<sup>th</sup> of april, 13<sup>th</sup> and 20<sup>th</sup> of may.

Finally meetings with the Health Department for the data return took place in July the 10<sup>th</sup> and 24<sup>th</sup> and in August the 7<sup>th</sup>.

## INTRODUCTION

Depression is a major cause of disability worldwide with high costs and consequences for individuals, families and society. World Health Organization (WHO) states that depression is the leading cause of disability as measured by Years Lived with Disability (YLDs) and the fourth leading contributor to the global burden of disease. By the year 2020, depression is projected to reach second place in the ranking of Disability Adjusted Life Years (DALYs) calculated for all ages (WHO, 2008).

Treatment for depression usually involves a combination of medication, talking therapies and self help. Pharmacological treatment is recommended for moderate or severe depression and is based mainly on antidepressants (AD). To achieve the best outcome, the process of prescribing should be evaluated as part of the Quality Assurance (QA).

QA was first developed in the early 60s in the fields of industry and public services in North America. It includes theories and procedures aimed at the control of products offered to consumers or users. In the healthcare field, quality has to deal with the optimal use of available resources (appropriateness and effectiveness), with the accessibility of services (equity) and with the satisfaction of patients (comfort) (Tavazza, 1988). As a matter of fact, the concept of quality is shaped according to each different stakeholders' perspectives. For health care professionals quality consists mainly in improving outcomes of patients. Administrators are concerned about the allocation of resources in terms of benefits to the whole population. Users, more and more aware of their rights, call for a greater weight in the decision-making process; for them, quality can consist in obtaining an improved state of health and an adequate satisfaction of their personal expectations. By combining these three perspectives, quality of care can be defined as the ability to improve the health and satisfaction of a population to the extent permitted by the technology, the resources available and the characteristics of the users (Palmer, 1988).

The concept of quality is therefore partial and the character of the knowledge acquired by the evaluation studies is particularistic, as it relates to the time and place of the assessment and is not necessarily transferable to the universe of health care. This should not be considered a limitation, but rather reflects the importance of clarifying objectives, purpose and possible consequences of the evaluation studies (Palmer, 1988).

If the goal of the quality assessment is to determine the extent to which medical practice is adequate to predefined standards (Donabedian, 1978), clinical audit is a quality improvement process aimed at improving patients care and outcome. Aspects of structure, process and outcome are selected and evaluated against explicit criteria. Where indicated, changes are implemented at an individual, team, or service level and further monitoring is used to confirm improvement in healthcare delivery (NICE, 2002).

In other words, clinical audit is a process by which health professionals maintain a regular and systematic review of their clinical practice and, where necessary, change it. Three main characteristics of the audit process have been pointed out:

- it is a continuous and systematic activity
- its main object is the appropriateness of processes (although it can be used to measure outcomes)
- it allows to measure the degree of inappropriateness (in excess and/or deficiency) and to identify which areas of professional practice shall be subject to improvement (Primary Health Care Clinical Audit Working Group, 1995).

Audit and feedback is often used in healthcare organisations together with other interventions, such as educational meetings or reminders (Ivers et al, 2012). Traditionally, the two elements that have been shown to be most effective in conducting an audit, are an environment where audit is made a priority by the trust board, so that it is encouraged and supported, and the existence of a structured programme for audit, where a trust has a central audit office that coordinates audit activity and brings together the results of audit for the trust as a whole (Benjamin, 2008).

Clinical audit entails benefits and disadvantages, facilitators and barriers.

A literature review (Johnston et al., 2009) has detected some perceived benefits:

- improved communication among colleagues and other professional groups
- improved patient care

- increased professional satisfaction
- better administration.

Some disadvantages have also been outlined:

- diminished clinical ownership
- fear of litigation
- hierarchical and territorial suspicions
- professional isolation.

The main barriers to clinical audit can be classified under five main headings:

- lack of resources
- lack of expertise or advice in project design and analysis
- problems between groups and group members
- lack of an overall plan for audit
- organizational impediments.

Besides, key facilitating factors were identified:

- modern medical records systems
- effective training
- dedicated staff
- protected time
- structured programs
- close interaction between purchasers and providers.

The authors concluded that clinical audit can be a valuable assistance to any program which aims to improve the quality of health care. Careful attention should be given to professional attitudes, yet without a coherent strategy valuable opportunities of change will be missed.

Among the instruments available to check and increase the appropriateness of their work, physicians can have recourse to audit on pharmaceutical prescriptions.

Albeit the main interest of the Health Authorities is the optimization of resources, nevertheless they often forget to provide prescribers of methodological instruments to change prescriptive behavior in a qualitative rather than quantitative way. Given these considerations, auditing of drug prescription may constitute a good response, not only on the practical, methodological or legal level but also to the best available evidence on a particular aspect of drug therapy (Grassi, 2007).

The author, in order to undertake a fruitful audit on drugs prescription, recommends to take into account that:

- drugs are to be prescribed only in relation to clinical needs
- simpler prescriptions are more likely to achieve better results
- the choice of the best available treatment must be based on efficacy and tolerability but also on costs.

The auditing activities must focus on the mechanisms of prescribing and not only on specific prescriptions. Some issues in drug prescription are of particular interest:

- under-prescription
- over-prescription
- choice of cost-effective drugs
- choice of effective treatment regimens
- monitoring the safe use of drugs
- monitoring costs
- adherence to treatment (compliance)

In addition to the pressures of healthcare institutions to contain the cost of care, cost-effective treatments are also an ethical issue, mainly when resources are particularly scarce, such as during economic crises. The use of generic drugs, for instance, allows savings without compromising qualitative standards. A high rate of prescription of generic drugs might be considered as an index of careful cost-effective approach and good clinical practice.



## *Antidepressant prescribing*

Antidepressant prescriptions have considerably increased in the last two decades all over the world, as documented by a large body of drug utilization research. Mc Manus et al., for example, considered the use of antidepressant (AD) drugs in the Australian community in the years 1990-1998 and compared these findings with those of other developed countries (Mc Manus et al, 2000). They measured the consumption of ADs in defined daily doses (DDD) per 1000 population per day. According to this analysis, the outpatient prescriptions increased in Australia from about 12.4 DDD/1000 population per day in 1990 to 35.7 DDD/1000 population per day in 1998. These data were compared to several major developed countries, including the United States, Canada, the United Kingdom, Sweden, France, Germany and Italy. The sales in the United States were almost identical to those in Australia in the same time period. The sales in Sweden and France were higher, and the sales in Canada and the United Kingdom were lower. The countries with the lowest usage levels (12 and 9.9 DDD/1000 population per day) were Germany and Italy. It was found that an increasing trend in AD prescriptions was emerging everywhere.

Moore et al. show that AD prescriptions, and specifically Selective Serotonin Reuptake Inhibitors (SSRIs), have been increasing in UK since the middle of the 1970s. From 2000 to 2005 prescribing of SSRI increased by 45% and accounted for half of all AD prescriptions and costs (Moore et al, 2013). The authors explore various explanations for the increased AD prescribing: different hypotheses were formulated, such as increased incidence, increased prevalence, increased care-seeking behaviour by patients and improved identification of depression by general practitioners. In fact, the majority of AD prescriptions resulted to be given as long-term treatment or to patients with multiple episodes of depression. This raises the question of discontinuation of antidepressants. It is established that patients are anxious regarding discontinuation of antidepressants and require support from their family doctor to stop medication. Patients not reviewed and supported are unlikely to initiate discontinuation on their own. On the other hand, guidelines recommend long term prescribing in patients with recurrent or relapsing depression (NICE, 2009) and an increase of prescribing may, therefore, be appropriate and may represent a better adherence to them (Anderson et al, 2008). However, a recent study involving detailed case review of patients on long term antidepressant prescription found that a significant proportion (56%) failed to meet criteria for a formal psychiatric diagnosis and that there was no indication for continued receipt of an antidepressant in nearly a third of participants (Cruikshank et al, 2008). Non-documented mental

health review over a two-year period was found in 21% of cases by another research (Petty et al, 2006). It has been hypothesized that the rise in antidepressant prescribing is mainly explained by the proportion of patients receiving long term treatment (Cruikshank et al, 2008) and suggested that future research has to focus on appropriate long term prescribing for depression and regular review of medication.

Recently a debate was held on BMJ about a crucial question: is the rise of ADs reflecting over-medicalization or is depression still under-recognised and under-treated?

From the first point of view (Spence, 2013) it is argued that over-medicalization is the consequence of current definition of depression, too loose, irrespective of circumstances and time. Since 75% of those who write these definitions have links to drug companies (Cosgrove et al, 2012), the relation with industry has engrained a therapeutic drug mindset to treat mental illness. Moreover, there is a lack in evidence concerning long term use to prevent relapse of depression, so that guidelines are more often “expert” opinions rather than evidence-based recommendations, with benefits still to be demonstrated.

The opposite position (Reid, 2013) asserts that ADs are not over-prescribed and their increase is due to a stricter adherence to guidelines concerning the duration of treatment. Meeting current guidance (at least six month of treatment) should improve outcomes but would eventually increase AD prescription volumes six-fold.

In summary, as commented by other authors, the rise in prescribing of ADs is largely accounted for by an increase in long-term treatment. People with risk factors for relapse of depression should be advised to continue with SSRIs for at least 12 months and consider long-term treatment (Reid and Barbui, 2010).

Besides, in many parts of the world the rise of AD use has been driven by a substantial increase in prescriptions by non-psychiatrists (Mojtabai et al, 2010), often for off-label indications. In this regard, it is to be noted that little is known about benefits for treating dysthymia and sub-threshold depressive symptoms or about serious adverse events, such as suicidality, seizures, increased bleeding and serotonin syndromes. Moreover, authors who reviewed the available literature (Cipriani and Barbui, 2009; Gartlehner et al, 2012) agree that routinely AD pharmacological treatment of sub-threshold and mild depression should be avoided.

Economic crisis is affecting most countries and evidence from a number of them shows that economic crisis and unemployment put mental health at risk since they act as chronic stressors producing a higher prevalence of depression (WHO Europe, 2003).

Hong et coll. (2011) studied the health inequalities in South Korea related to the country's economic crisis in the late 1990s. The authors showed the existence of significant pro-rich inequalities in the prevalence of depression, suicidal ideation and suicide attempts. The inequalities in each instance have doubled over the past ten years, accompanied by widening income inequality following the nation's economic crisis in the late 1990s.

Cascade et coll. (2009) investigated in USA total prescription and new prescription trends before and after the economic slowdown beginning in September 2008. Both total prescriptions and new prescriptions for sleep aids, benzodiazepines and antidepressants increased. There appears to be a small spike in the number of total and new prescriptions following September 2008, although this increase was not enough to cause a statistically significant change in the overall rate of increase of prescriptions over time.

In Italy, as well as in other countries with economic depression, spending reviews decrease the health budget. Given that even in high income-countries the budget for mental health is more and more limited, decision-makers need to consider the relative cost-effectiveness of alternative uses of available resources.

Appropriateness and cost-effectiveness of treatment of depression are major issues and still an open field of discussion. Since the start of the era of newer ADs, such as SSRIs and SNRIs, many RCTs comparing antidepressants have concluded with a "me too" sentence, finding out efficacy not superior to the previous ADs.

In the STAR-D study (Rush et al, 2006) the outcome measure was remission of depressive symptoms, e.g. becoming symptom-free. Citalopram achieved remission rates of 35-40% and a clinical response in 50-55%. Among treatment-resistant patients, 25% had remission switching to another AD like Bupropion, Sertraline or Venlafaxine. None of them has proved to be a better second choice than the others.

This is particularly important since more than a dozen of ADs have been approved by regulatory agencies (e.g., FDA, EMA, AIFA) on the base of trials assessing the superiority of the new AD

towards placebo. Nearly all studies looked at outcome after 6-8 weeks and could only assess whether patients had a reduction in some symptoms as a response to treatment (Insel, 2011).

Recent meta-analyses show controversial conclusions in terms of efficacy and side effects.

A multiple-treatment meta-analysis (Cipriani et al, 2009) reviewed 117 RCTs with 25928 participants to assess efficacy and tolerability of 12 new-generation ADs on major depression. The major findings were that the significantly more efficacious ADs were Sertraline, Mirtazapine, Escitalopram and Venlafaxine. On the other hand, Escitalopram, Sertraline, Citalopram and Bupropion displayed a better tolerability. Therefore, both Sertraline and Escitalopram were found to have the best efficacy-tolerability profile, but Sertraline is much cheaper than Escitalopram. Interpretation of data was that Sertraline might be a better choice when starting treatment for moderate to severe major depression in adults because it entails the most favourable balance between efficacy, adverse reactions and acquisition cost.

Another meta-analysis reviewed 203 studies (Gartlehner et al, 2011) to compare efficacy and side effects of second generation ADs. The conclusion of the authors was that current evidence does not warrant the choice among second-generation ADs on the basis of differences in efficacy, whilst other properties, namely onset of action and adverse events, may be crucial, as well as taking into account the characteristics of the patient. On these premises, US consumer associations developed recommendations for less expensive generic drugs with well-established safety profiles like Bupropion, Citalopram, Fluoxetine, Paroxetine and Sertraline (Best Buy Drugs Consumer Report, 2011).

However, while the debate on comparative efficacy and tolerability is still going on, the expiration of the patent of many ADs provides the possibility of saving resources that can be re-allocated.

### ***The use of antidepressants in Italy***

Over the last few years Italian data have shown a significant increase of the use of ADs, attributable either to the increasing prevalence of depression and other common psychiatric disorders as anxiety, or to the greater tolerability of second generation ADs, that have become the first choice ADs and have largely overtaken older ADs.

The OSMED report 2011 notes that in Italy the three most frequently prescribed ADs are Paroxetine, Escitalopram and Sertraline. Escitalopram, a branded SSRI still protected by patent, shows a further increase in prescription of 6.9% compared to 2010 and ranks on the 16<sup>th</sup> place (141 million euro) of the most prescribed drugs. In quantitative terms, the prescription (7.3 DDD/1000 persons/day) is similar to Paroxetine and superior to Sertraline, with a cost much greater than the other two compounds. Duloxetine, another branded antidepressant (SNRI) protected by patent and the only one with an indication for treatment of pain in diabetic polyneuropathy, shows an increase in the prescription compared to 2010 (+5%) and accounts for 2.3 DDD/1000 persons per day (OSMED, 2012).

## ***AIMS OF THE AUDIT: ADDRESSING APPROPRIATENESS AND REDUCING COSTS***

In this national context, the Local Health Authority (LHA) of Bologna presents higher prescriptive levels of ADs than the average of Emilia-Romagna Region (**Table 1 page 22**), which is in turn among the Italian Regions with the highest outpatient consumption of ADs (OSMED, 2012). In particular, the prescription of SSRIs rose in Bologna by 11% from 2007 to 2011. This increase is aligned to that of the whole Emilia-Romagna Region (Poluzzi et al, 2013).

Escitalopram and Duloxetine represent together about a quarter of the whole outpatient AD prescribing in Bologna LHA, accounting for almost half of the ADs cost.

In fact, these two ADs are much more expensive than others whose patents have expired, even though no conclusive proof of their superior efficacy and safety emerges from meta-analyses of clinical trials (Cipriani & Barbui, 2009; Gartlehner et al., 2012).

**TABLE 1 – Consumption and cost of antidepressant outpatient treatments in Emilia-Romagna (RER). Comparison across Local Health Authorities (Year 2011).**

<b>AD prescriptions 2011</b>	<b>DDD/1000 inhab/day</b>	<b>Euro/inhab</b>
<b>Piacenza</b>	36,13	7,87
<b>Parma</b>	47,28	9,93
<b>Reggio Emilia</b>	40,11	8,11
<b>Modena</b>	44,58	9,41
<b>Bologna</b>	<b>46,63</b>	<b>10,07</b>
<b>Imola</b>	40,38	8,38
<b>Ferrara</b>	45,92	10,80
<b>Ravenna</b>	49,85	10,40
<b>Forlì</b>	42,88	9,11
<b>Cesena</b>	43,46	9,42
<b>Rimini</b>	36,11	7,78
<b>Average RER</b>	<b>43,89</b>	<b>9,31</b>

The main international guidelines (NICE, 2009; Qaseem et al, 2008) recommend that besides efficacy and safety also cost should be taken into consideration when choosing the AD treatment. According to NICE guidelines, for instance, prescriptions of ADs for treating major depression should start with a SSRI in generic form. Actually, drugs with expired patents can bring other important advantages to clinical practice besides lower costs, since they have generally been longer in use and are better known as regards pharmacological characteristics, efficacy and side effects than newer agents.

Therefore, it has been considered a priority for the LHA of Bologna to reduce prescriptions of Escitalopram and Duloxetine, with the aim to decrease the cost of AD treatments without compromising efficacy and tolerability. Consequently, local recommendations propose that the use of these two drugs should be restricted to patients who did not respond to previous treatment or who experienced side effects with other ADs or, as regards Duloxetine, suffer from pain in diabetic neuropathy.

In order to achieve this goal, the audit methodology was considered suitable, involving general practitioners as well as psychiatrists working in Community Mental Health Centres or in licensed private hospitals. In October 2012 an audit process was hence activated, involving LHA psychiatrists and general practitioners, as well as experts from the Clinical Governance Unit and the Pharmaceutical Department and a Primary Care medical manager. The audit team was set up (9 psychiatrists, 5 general practitioners, 5 members from the Clinical Governance Unit, the Pharmaceutical and the Primary Care Departments) and the first meetings were held to examine and discuss LHA performances on AD prescribing.

The following sections present the experience carried out so far, with an overview of standards to be addressed, actions implemented, benefits and facilitating factors detected, along with drawbacks, limitations and obstacles encountered.

## METHODS

### *Setting and data sources*

In the Italian Health System, LHAs are responsible for the services offered to well-defined catchment areas. Primary care, placed at the heart of the health system, is free of charge for patients and has a pivotal role in the management of patients with chronic diseases, including mental illness. General practitioners (GPs), who are independent contracted professionals operating under the control of LHAs, are the point of entry into the healthcare system and act as gatekeepers for access to specialty and hospital care. Mental Health Departments (MHDs) are in charge of the management and planning of all activities related to prevention, treatment and rehabilitation of mental disorders. Within the MHDs, Community Mental Health Centres (CMHCs) are concerned with interventions pertaining to adult psychiatry in outpatient, rehabilitative and residential settings, while acute inpatient care is provided by general hospital psychiatric units.

The Bologna LHA covers a mixed urban-rural area including the main regional city and serves a population of approximately 850,000 inhabitants, roughly one fifth of the population of the Emilia-Romagna Region. The Primary Care Department (PCD) encompasses 41 Primary Care Units (PCUs), composed by 624 GPs along with other health professionals (paediatricians, nurses, social workers, etc.). In the local MHD, 11 CMHCs are evenly distributed throughout the catchment area.

In order to improve the appropriateness of prescriptions, it is necessary to promote collaborative care and integrated training between the PCD and the MHD. In this regard, an important attempt to promote the integration between primary care and mental health services is represented by the ‘G. Leggieri’ Program, started in 2000 as an effort of the Health Government of Emilia-Romagna Region to coordinate initiatives of primary care-mental health cooperation. In particular, a main objective was identified and pursued, to improve the quality of treatment for patients with common psychiatric disorders in primary care. In the framework of this program, regional recommendations were delivered according to the stepped care model proposed in the NICE guidelines (NICE, 2009). Stepped care is a system of healthcare based on treatments of differing intensity graded to the patient’s needs, so that the least intrusive or restrictive intervention is first provided. Within this regional context, PCD and MHD in Bologna have gained a long lasting collaborative experience, given that since the 90s they have taken to meeting in PCUs for clinical supervisions and integrated

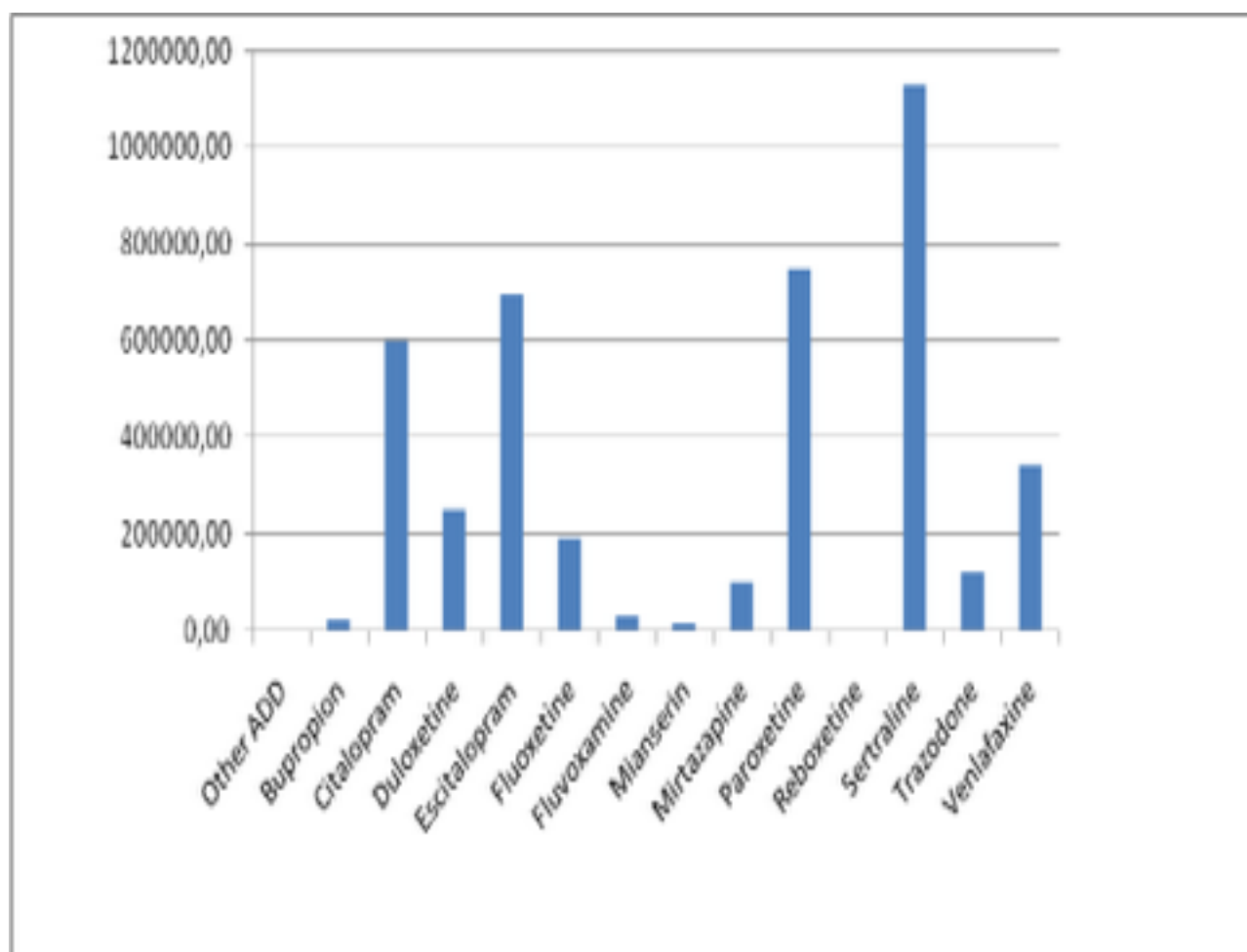


training.

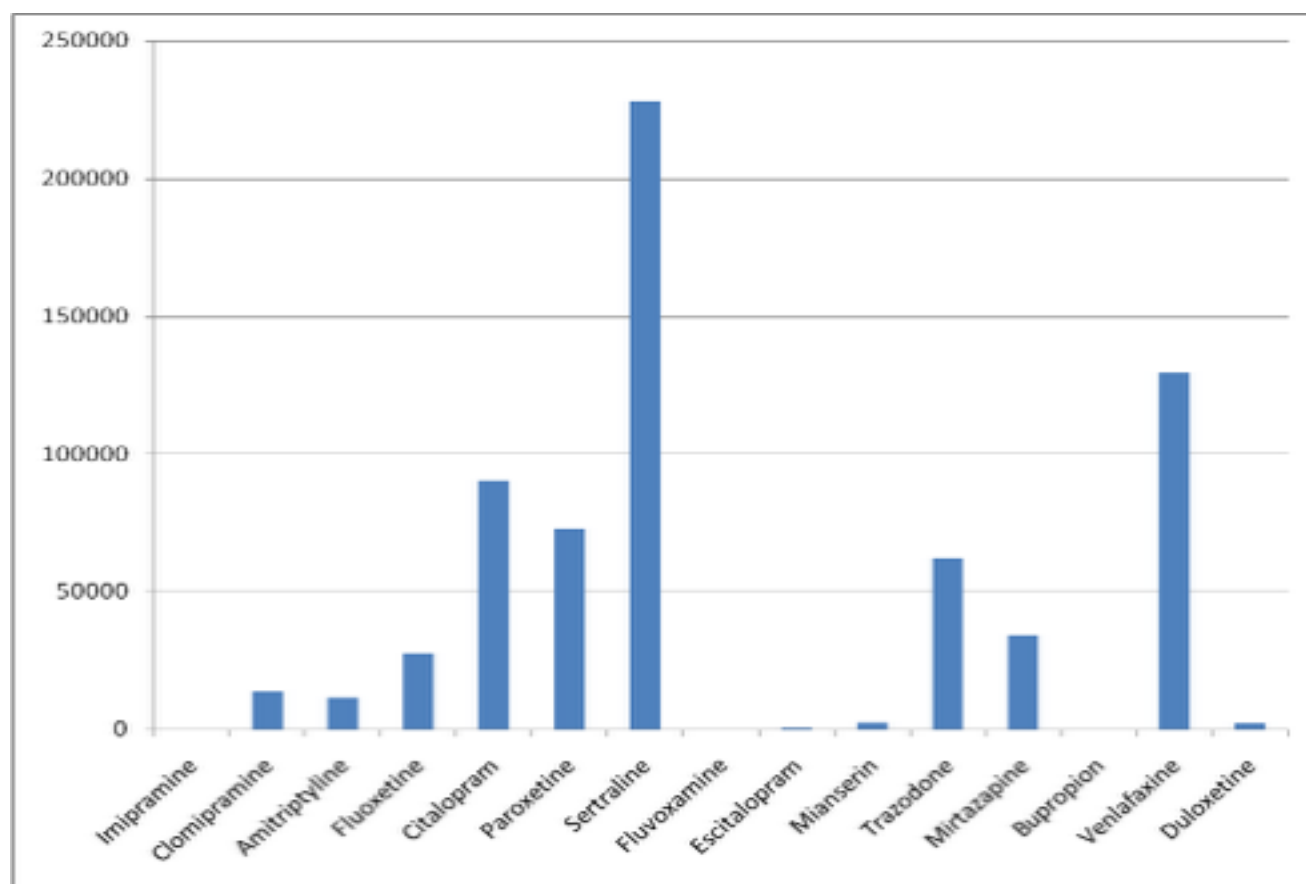
In the first stages of the audit cycle, a survey was carried out to describe the baseline situation in AD prescribing. Data of AD use in the first four months of 2012 have been extracted from two LHA databases:

1. **Outpatient Pharmaceutical Database (OPD):** collects drugs prescriptions covered by the National Health System (**Figure 1 page 26**). Prescriptions of GPs and Psychiatrists CMHCs have been extracted (prescriptions of other specialists like neurologists or geriatricians, representing a percentage of about 3% of the total, are not included). The greatest part of the AD prescriptions is due to the GPs (95,4% against 4,6% of the psychiatrists).
2. **Hospital Drug Supply Database (HDSD):** drugs are directly distributed from CMHCs, from the direct distribution points of the pharmaceutical department, from hospitals, from residential facilities or distributed “on behalf” in the public or private pharmacies. Only ADs included in the Emilia-Romagna Regional Formulary are allowed to be administered or distributed. The HDSD does not entail patient-centred data during hospital stay. However, the hospital consumption of ADs represents only a small part of the total consumption in the LHA of Bologna. In fact, the use of AD depends mainly (more than 85%) on prescriptions for outpatients treatment collected in OPD (**Figure 2 page 27**).

**Figure 1 Outpatient prescriptions in the LHA of Bologna: consumption of antidepressant drugs (DDD) prescribed by General Practitioners (first four months 2012).**



**FIGURE 2 Hospital Drug Supply in the LHA of Bologna: consumption (DDD) of antidepressant drugs (first four months 2012).**



Drugs are codified by the Anatomical Therapeutic Classification (ATC, ver. 2011) (WHO Collaborating Centre for Drug Statistics Methodology, 2011).

The Defined Daily Dose (DDD) is a definition of the mean dosage of a drug assumed daily by an adult. Using DDD data can be expressed like “numbers of conventional days” of prescribed therapy: this makes comparable drugs used at different dosages (diverse pharmacological potency) and is independent from pharmaceutical preparations.

The ratio between DDD consumed and number of inhabitants per day (number of DDD per 1000 inhabitants per day) allows to:

- compare prescription volumes in different populations

- obtain a rough estimate of the exposition in a population to a certain drug or class of it.

For example, if in a certain area 50 DDD have been prescribed per 1000 inhabitants per day, we can assume that 50 persons per 1000, i.e. 5%, receive one DDD of that drug every day.

The resident population refers to 01/01/2011.

The population of PCUs is obtained by summing the number of GPs' enrolled patients in each PCU.

### ***Comparison of current practice with standard care***

NICE guidelines on depression have been chosen as reference recommendations for standard care (NICE, 2009).

According to NICE guidelines, a SSRI in generic form should be recommended as first AD choice. Generic SSRIs included in the Emilia-Romagna Regional Formulary (Fluoxetine, Paroxetine, Sertraline and Citalopram) should be selected, if not otherwise requested for specific clinical reasons.

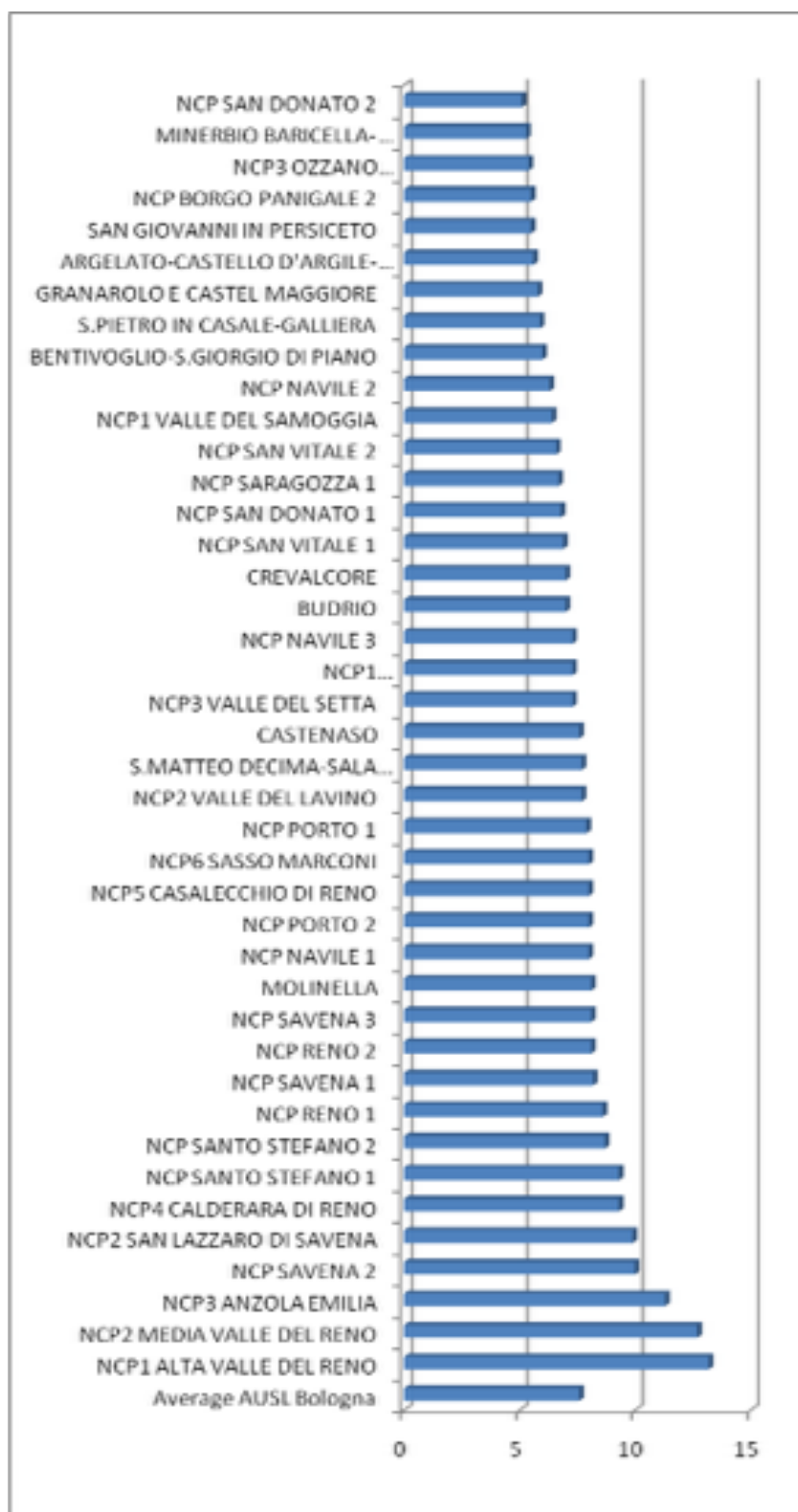
The audit team collected, reported and discussed the LHA consumption data on ADs in the first four months of 2012. The principal findings to be pointed out, were the following:

- The outpatient consumption of AD was by far greater than the inpatient one, representing over 85% of the total consumption, as measured by the international standard of DDD.
- The outpatient prescriptions of ADs were almost entirely attributable to GPs (92%), compared to 5% due to CMHCs psychiatrists and to the 3% of other specialists.
- Even if Escitalopram and Duloxetine are not listed in the Emilia-Romagna Regional Formulary, they made together almost half (46%) of the cost of AD outpatient medications; the expenditure exceeded greatly 1 million euro in the first four months 2012 and approximately 3,500,000 euro were predictable over an year span, i.e. more than 3 million DDD.
- Escitalopram and Duloxetine were unevenly prescribed across the PCUs of the LHA. Consumption was compared through the 41 PCUs of the LHA (DDD/1000 inhabitants/day). A greater use of the two drugs in the mountainous surroundings and in the east side of the city has been found. However, it has been observed that the profile of prescriptions was not

the same for Escitalopram and Duloxetine across the PCUs: e.g., in the PCUs of the Porretta Health District the prescription of Duloxetine was not as high as the use of Escitalopram.

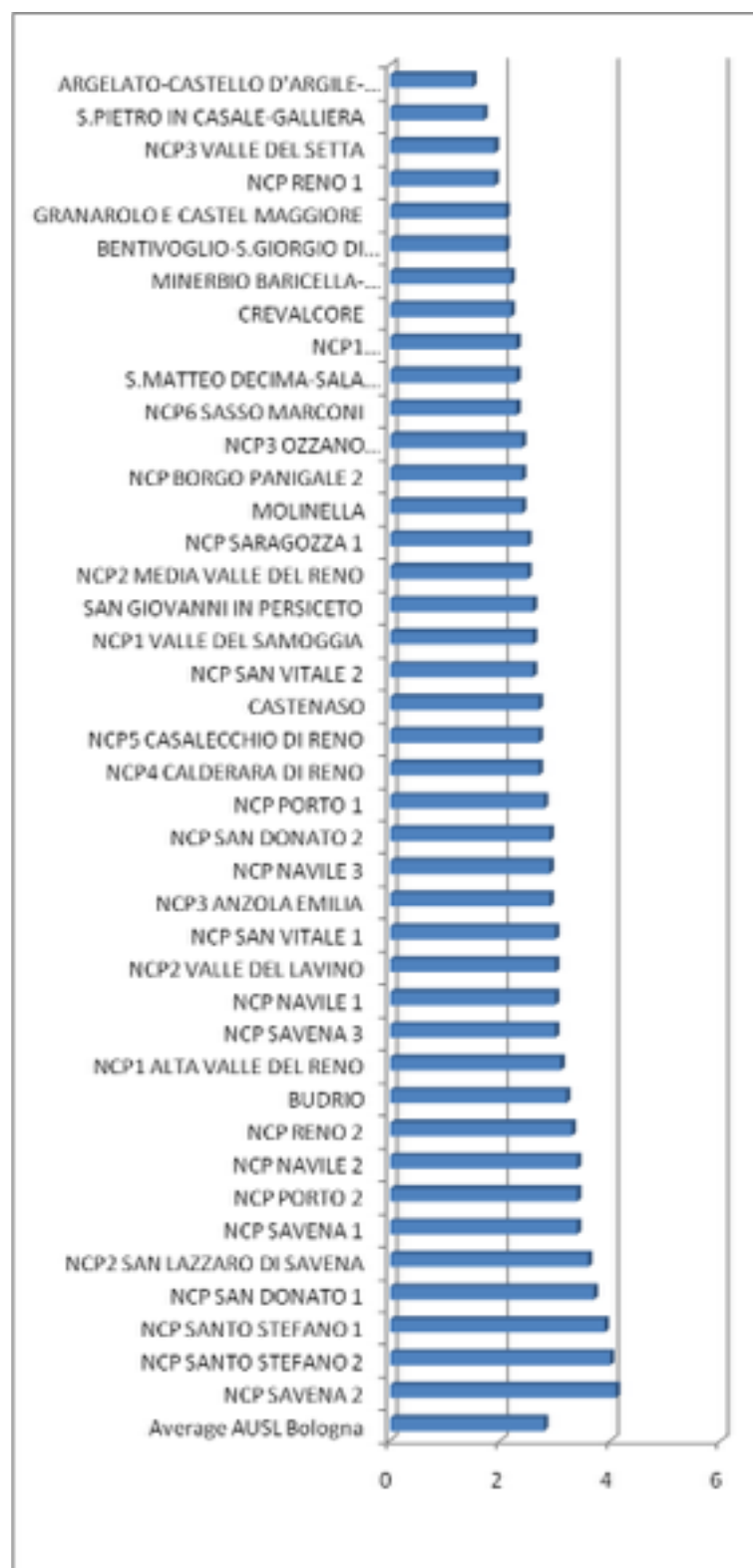
- The comparison of the prescription attitudes showed a considerable variability of the amount of Escitalopram prescribed by GPs, ranging from 5.1 DDD/1000 inhabitants per day in the urban PCU of San Donato to 13.2 in the mountain PCU of Alta Val di Reno (**Figure 3 page 30**). After consolidation of prescribing data into each health district, the consumption of Escitalopram was confirmed proportionally higher in the mountain health district of Porretta, reaching an average of 10.9 DDD/1000 inhabitants/day. Next to them there were the East district of the city of Bologna, the suburban district of S. Lazzaro and the rural one of S. Giovanni.

**FIGURE 3 - GPs' prescriptions in the LHA of Bologna: consumption of Escitalopram (DDD) in each PCU (First four months 2012).**



- The map of consumption of Duloxetine was partly different (**Figure 4 page 32**): the East area of the city showed the highest prescription quota (3.9 DDD/inhab./day), followed by the other urban districts. The prescriptions in the East area of Bologna were more than twofold the rural district of Reno-Galliera (1.8 DDD/inhab./day).

**FIGURE 4 - GPs' prescriptions in the LHA of Bologna: consumption of Duloxetine (DDD) in each PCU (First four months 2012).**





- Psychiatrists, although achieving a total number of prescriptions of AD much lower than GPs, prescribed more often Escitalopram and Duloxetine: 36% of the DDD of ADs recorded in OPD by psychiatrists consisted in Escitalopram and Duloxetine, representing 58% of the expenditure (**Table 2**). It has to be noted that a proportion of psychiatrists' prescriptions is usually carried out in CMHCs, through direct distribution of drugs to patients, and then recorded in HDSD.

**TABLE 2 – Consumption and cost of Escitalopram and Duloxetine. Outpatient prescriptions (first four months 2012).**

DDD of Escitalopram and Duloxetine	DDDs Escitalopram	DDDs Duloxetine	DDDs Escitalopram + Duloxetine
Prescriptions by GPs	696.03	255.084	951.114
Prescriptions by CMHC psychiatrists	47.380	25.627	73.007
<b>Total</b>	<b>743.410</b>	<b>280.711</b>	<b>1.024.121</b>

DDDs	€ Escitalopram	€ Duloxetine	€ Escitalopram+ Duloxetine
Prescriptions by GPs	605.582	478.133	1.086.716
Prescriptions by CMHC psychiatrists	42.041	49436	91.477
<b>Total</b>	<b>650.623</b>	<b>527.569</b>	<b>1.178.192</b>

- As regards CMHC psychiatrists' prescriptions of Escitalopram and Duloxetine, the distribution appeared variegated. Regarding Escitalopram, the highest values of DDD were recorded in two CMHCs of the West side of the city, followed by two East located suburban and rural CMHCs. In turn, Duloxetine showed the highest values in two urban CHMCs.
- The analysis of the amount of the two drugs prescribed by each psychiatrist highlights the relevant variability of prescriptions among teams as well as within teams.
- The PCUs and the CMHCs with higher levels of consumption of Escitalopram and Duloxetine were located in different areas.
- About 5% of patients with Duloxetine prescriptions were also prescribed an anti-diabetic drug and are presumably diabetic.

Overall, we can argue that such a high prescription of Escitalopram (16.6% of the total DDD for ADs) and Duloxetine (6.3%) is not reserved for cases of major depression resistant or intolerant to other treatments (or, as regards Duloxetine, for patients with diabetic neuropathic pain) and is therefore to consider inappropriate in relation to the NICE guidelines.

Moreover, the erratic usage of the two branded ADs is itself a strong indicator of inappropriateness. Actually, whether or not there are well-established standards, it is generally accepted that high variability of prescriptions across neighbouring areas, not otherwise explained by epidemiological causes, reveals inappropriate use of drugs (Mazzaglia, 2008).

## THE AUDIT PROCESS

NICE guidelines were selected by the audit team as reference recommendations. In addition, a narrative review of clinical trials, meta-analyses and guidelines on AD drugs, was completed by some facilitators and made available on the LHA intranet for the whole team. Scientific evidence was then discussed during the following meetings, finding a substantial consistency as regards the main issues.

Criteria and standards were then developed, in order to define the outcome to be measured.

Limitations in information systems did not allow to extract individual patient records in order to identify first AD prescriptions. It was therefore decided to measure the percentage of Escitalopram and Duloxetine DDDs of the total amount of outpatient AD prescriptions. On the basis of the reported consumption data, standards to be achieved were then defined as:

- 1) a reduction of 20% in Escitalopram and Duloxetine prescriptions.
- 2) a decrease of 30% in the range of variability among PCUs in Escitalopram and Duloxetine consumption.

Some critical aspects were identified as obstacles to change the prescriptive attitudes.

In particular, four critical areas were found to be relevant for the success of the audit.

Since changes in practice may be achieved more effectively by involving several different types of action (NICE, 2002), the audit group worked out a strategy to solve these aspects with a time schedule as described below:

1. Insufficient involvement of colleagues working in private licensed hospitals, public psychiatric wards and residential facilities.

Actions undertaken:

- Two colleagues of hospital/residential wards were integrated into the audit team.

## 2. Inadequate awareness of CMHCs psychiatrists.

### Actions undertaken:

- The goals of the audit were discussed with clinicians in charge of services: audit team members attended MHD coordination meetings and presented findings of preliminary report as well as scientific evidence and guidelines on ADs (November 2012 - March 2013).
- Meetings with CMHCs staffs were held in order to present the audit and its goals, to discuss scientific evidence and to provide each psychiatrist with a baseline report on their own AD prescriptions referred to the first four months 2012 (November 2012 – March 2013).

## 3. Scarce communication of the goals of the audit and of the economical and scientific rationale.

### Actions undertaken:

- A leaflet summarizing evidence and objectives of the audit (**Figure 5 page 38**) was prepared (November 2012 – January 2013). Then it was first handed out to CMHC medical managers to favour psychiatrists' involvement through panel discussions in each CMHC. Later, the leaflet was presented and discussed by the LHA advisor during his outreach visits to CMHCs and GPs (see below).

## 4. Different levels of communication and training with GPs through PCUs.

### Actions undertaken:

- An e-mail service was set up to allow feedback, request for explanations or scientific data (November 2012).
- Outreach visits to GPs and psychiatrists by a LHA drug adviser were carried out between January and May 2013
- Small-scale educational meetings in each PCU were addressed to a maximum of 25 GPs, focusing on NICE 2009 guidelines and scientific literature. The training sessions were carried out in March 2013 and were held by CMHC psychiatrists, in some cases with the collaboration of CMHC nurses. During these interactive meetings, feedback

reports were delivered by PCUs managers to each GP.

Actions were implemented between November 2012 and May 2013.

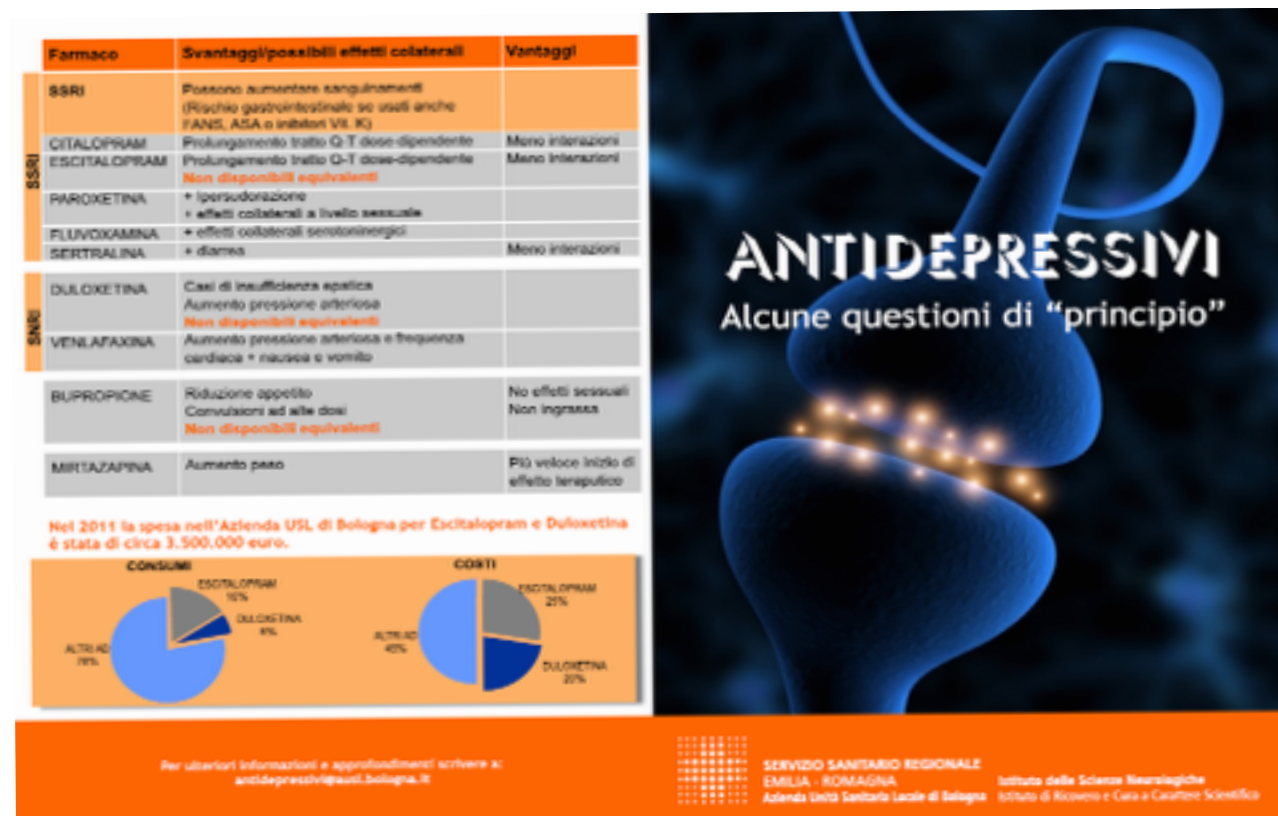
Prescriptions data related to the post-implementation stage, i.e. to the four months June – September, are expected for a comparison with the baseline pre-implementation stage in November 2013.

However, preliminary feedback data related to the period March–June 2013 were provided by the Pharmaceutical Department in August 2013.

As regards CMHC psychiatrists, a 51% decrease in Escitalopram DDD and a 42% decrease in Duloxetine DDD were detected. It is noteworthy that a total AD marked decrease in outpatient consumption has been observed, ranging from 205,495 DDDs in the first four months 2012 to 147,208 in March-June 2013 (-28%). This reduction in psychiatrists' outpatient prescriptions was more than counterbalanced by a far greater increase in DDDs distributed in CMHCs and hospitals (+ 98,244 DDDs in the four-month 2013 period). We must remember that direct distribution in LHA facilities involves only ADs included in the Regional Formulary, with the exception of patented ADs such as Escitalopram and Duloxetine.

As for GPs, differences between 2012 and 2013 in prescribing performances were much lower. On the whole, a 10% decrease in Escitalopram and a 2% in Duloxetine usage were recorded, while the total AD consumption remained stable.

FIGURE 5 – The LHA leaflet on antidepressant prescription



### SCEGLIERE L'ANTIDEPRESSIVO

Discutete con il paziente la scelta dell'antidepressivo (AD), prendendo in considerazione:

- Eventi avversi (effetti collaterali e sintomi da interruzione)
- Potenziali interazioni con farmaci concomitanti o malattie fisiche
- Percezione del paziente dell'efficacia e della tollerabilità di AD precedentemente assunti

Utilizzate come prima scelta un Inibitore Selettivo del Re-uptake della Serotonina (SSRI) a brevetto scaduto. Tenete conto che:

- Gli SSRI comportano un maggior rischio di sanguinamento, in particolare del tratto gastro-intestinale. Prendete in considerazione di prescrivere un gastroprotettore in pazienti anziani che stanno assumendo anche FANS o aspirina.
- Fluoxetina, Fluvoxamina e Paroxetina hanno un maggior potenziale di interazioni farmacologiche.
- Citalopram o Sertralina hanno un minor potenziale per interazioni farmacologiche e quindi sono da preferire in pazienti con comorbidità intermistiche croniche.
- Paroxetina presenta una maggior incidenza di sintomi da sospensione.

Tenete conto della tossicità in overdose per le persone con rischio significativo di suicidio. Triciclici e Venlafaxina hanno un rischio più alto di morte per overdose rispetto ad altri AD.

Quando prescrivete AD diversi dagli SSRI, ricordate che: Venlafaxina, Duloxetina (che sono inibitori del Re-uptake di Serotonina e Noradrenalina (SNEI)) e Triciclici hanno un rischio maggiore di interruzione del trattamento per effetti collaterali. Di conseguenza occorre aumentare le dosi gradualmente!

Raccomandazioni estratte e tradotte da: Users Guide NICE Depression, 2009

### DOPO UNA RISPOSTA INCOMPLETA O INADEGUATA AL TRATTAMENTO INIZIALE:

Controllate che il farmaco sia stato assunto come prescritto.

Se la risposta è assente o minima dopo 2-4 settimane:

A) SE NON CI SONO EFFETTI COLLATERALI:  
aumentate il dosaggio fino al massimo consentito

B) SE CI SONO EFFETTI COLLATERALI O SE IL PAZIENTE PREFERISCE:  
passate a un altro AD

Se c'è qualche miglioramento entro 4 settimane:

continuate per altre 2-4 settimane e poi rivalutate

SE LA RISPOSTA NON È ANCORA ADEGUATA, O CI SONO EFFETTI COLLATERALI, OPPURE IL PAZIENTE PREFERISCE CAMBIARE FARMACO:

passate a un altro AD

### QUANDO PASSATE A UN ALTRO AD, CONSIDERATE:

- Inizialmente un diverso SSRI
- Successivamente, scegliete un antidepressivo di una classe differente con una tollerabilità inferiore (come Venlafaxina o un Triciclico)

Abituamente con gli AD con emivita breve potete effettuare il cambiamento di AD entro una settimana.

Considerate le interazioni e fate attenzione quando passate:

- da Fluoxetina ad altri antidepressivi
- da Paroxetina o Fluoxetina a un Triciclico. Iniziate con una dose base di Triciclico

Evitate associazioni di Antidepressivi

(Il Medico di Medicina Generale può eventualmente richiedere consulenza specialistica).

Per consultare la linea guida sul sito NICE:  
<http://guidance.nice.org.uk/CG90>

Non vi sono evidenze certe che ESCITALOPRAM e DULOXETINA offrano più vantaggi clinici di altri antidepressivi.

È certo che Escitalopram e Duloxetina sono più costosi degli altri antidepressivi a brevetto scaduto.

Per questi motivi l'utilizzo di Escitalopram e Duloxetina va possibilmente riservato ai casi che non hanno risposto ad altri antidepressivi o che hanno manifestato reazioni avverse.

Duloxetina ha indicazione anche per il trattamento del dolore da neuropatia diabetica.

## DISCUSSION

There is conflicting evidence on whether audit works. As noted by some authors, audit and feedback has not consistently been found to be effective (Benjamin, 2008).

A recent Cochrane Collaboration review stated that audit and feedback generally leads to small but potentially important improvements in professional practice. The quality of the evidence was moderate, and showed that audit and feedback may be most effective when: 1) the health professionals are not performing well to start out with; 2) the person responsible for the audit and feedback is a supervisor or colleague; 3) it is provided more than once; 4) it is given both verbally and in writing; 5) it includes clear targets and an action plan. Overall, the effectiveness seems to depend on baseline performance and how the feedback is provided (Ivers et al, 2012).

Our preliminary data need to be further examined, split into PCUs and confirmed by outputs related to the whole post-implementation period. At first glance, since the audit impact seems lower among GPs than psychiatrists, GPs appear to disclose a slower attitude to change AD prescribing patterns. Consistently with recommendations (Benjamin, 2008; Ivers et al, 2012), this hypothesis can encourage us to go on with shared training, supervision and collaborative care between PCD and MHD. Moreover, developing specific mechanisms and systems to monitor and sustain improvement once the audit cycle has been completed, should entail reminders to be regularly be prompted to GPs, periodic educational meetings in each PCU, provision to each GP of individual reports on AD prescriptions, with comparisons between present period and baseline observation.

One of the most relevant aspects of the audit process concerns communication skills and the obstacles to change the prescriptive attitudes.

At this regard, Grol highlights the importance of theories underlying different approaches to implement guidelines and change practice. Distinction must be made between approaches focusing on internal or external influences (Grol, 1997):

Focus on internal processes:

- Educational
- Epidemiological
- Marketing

Focus on external influences:

- Behavioural
- Social interaction
- Organisational
- Coercive

The author states that no method is definitely superior. Different change proposals (guidelines, research findings, new procedures) may demand different implementation strategies. Different groups of clinicians will experience different obstacles or may function at different levels of tackling change. Implementing changes is usually not a single action but involves a well planned stepwise process, including a combination of interventions, linked to specific obstacles to change. In conclusion, all the different approaches for changing clinical practice may be valid and effective, provided that they are adapted to the specific features of the change proposed, to the target group, the setting, and the obstacles encountered. The most practical advice to individuals responsible for changing and improving practice is to be aware of their own assumptions about human behaviour and change.

The barriers described in the aforementioned literature emerged also from this audit and have pushed to develop a model to identify obstacles, to link interventions to obstacles, to carry out planned actions and to evaluate results achieved.

The principal barriers to change prescriptive patterns in the LHA of Bologna have resulted to be:

- scepticism towards clinical evidence in scientific literature;
- tendency to favour personal experience and word of mouth among colleagues rather than guidelines indications;
- influence of marketing.

Clinicians have expressed sceptical opinions on clinical trials, convinced that results can be potentially biased by many confounding factors, and that meta-analyses can be invalidated by methodological flaws, as well as by sponsorship, selection and publication biases. Therefore, guidelines evidence-based have been criticized too. To overcome this scepticism and the “experience vs. evidence” dichotomy, a fruitful strategy has consisted in small-scale educational meetings, held by psychiatrists of the audit team to their colleagues, which in turn conducted other meetings with GPs. In this regard, meetings where some meta-analyses were commented critically by the LHA prescribing adviser and audit team members, seemed to be particularly appreciated and useful.

The influence of marketing has been hypothesized, mainly by reason of the high prescriptive variability across different areas of the LHA, not otherwise explicable.

In Italy, the total national expenditure on pharmaceuticals (including drugs distributed through public and private pharmacies and those purchased and dispensed by public health facilities), amounted to over 19.2 billion euro (Brunetti M, 2006). The Italian Pharmaceutical Manufacturers Association indicates that, in Italy, 3,000 billion euro (15 percent of the revenue) is spent on promotion. In front of total pharmaceutical expenditure, taking an average of all 367,000 registered



doctors, the industry 'invests' for each physician about 8,000 euro per year.

Similar estimates are described in most countries in the world. Pharmaceutical companies in the United States spent in 2004 about 57.5 billion dollars, i.e. 24.4% of their revenue, on promotion (Gagnon and Lexchin, 2008). An estimate of total promotional expenditure in France in 2004 is 2,908 million euro (12.2% of revenue). However, another estimate is that pharmaceutical detailing cost 3,300 million euro and accounted for 75% of the overall cost of promotion in that year making promotion 17.3% of revenue (Bras et al, 2007).

A systematic review (Spurling et al, 2010) searched for studies on physicians who were exposed to information from pharmaceutical companies and measured outcomes like quality, quantity and cost of prescribing. Due to limitations of studies reported, the authors were unable to reach any definitive conclusions about the degree to which information from pharmaceutical companies increases, decreases, or have no effect on the frequency, cost, or quality of prescribing. No evidence of net improvements in prescribing was found, but the available literature does not exclude the possibility that prescribing may sometimes be improved. Still, authors recommend that practitioners follow the precautionary principle and thus avoid exposure to information from pharmaceutical companies.

A similar review was made in Portugal (Granja, 2005) to explore the so-called “dangerous liaisons” between physicians and pharmaceutical representatives. Interactions between physicians and detailers (even when legitimate ones) raise scientific and ethical questions. The author searched for self-perception of physicians and how they see themselves when interacting with pharmaceutical companies and their representatives. Do these companies in fact change their prescriptive behaviour, and, if so, how do they change it? How can physicians interact with detailers and still keep their best practice?

The frequency at which Portuguese physicians (especially family physicians) contact with pharmaceutical representatives is higher than the frequency reported in countries where the available studies come from (namely, Canada and the United States of America). Most physicians hold firmly to the belief that they are able to resist and not be influenced by drug companies promotion activities. The author concluded that representatives effectively promote drug sales, that the information they provide to physicians may be largely incorrect and that there is time to start a debate.

Awareness is growing that interaction with pharmaceutical sales representatives is a question deserving careful ethical analysis. Brody formulated the issue in the following way:

- It is a matter of professional integrity.
- It is highly likely to behave in ways contrary to professional principles when in relationship with representatives.
- Professional responsibilities do not require to keep contacts to representatives.

- Physicians must choose if adhere to professional principles.

The author's conclusion is that physicians ought to refuse to visit with representatives in reason of both professional integrity and sensible time management (Brody, 2005).

If it is apparent that there can be a conflict of interest between marketing and optimal patient care, little is known about how physicians resolve this contradiction.

Chimonas et al. explored the dynamics of the relationship between physicians and representatives with the purpose to determine physicians' techniques for managing cognitive inconsistencies within their relationships with drug representatives. The authors found that physicians understood the concept of conflict of interest and applied it to relationships with detailers. However, they maintained favourable views of physician-detailer exchanges. Holding these mutually contradictory attitudes, physicians were in a position of cognitive dissonance. To resolve the dissonance, they used a variety of denials and rationalizations:

- avoiding thinking about the conflict of interest
- disagreeing that industry relationships affected physician behaviour
- denying responsibility for the problem
- enumerating techniques for remaining impartial
- recognising that meetings with detailers were educational and benefited patients.

The authors concluded that although physicians understood the concept of conflict of interest, relationships with detailers set up psychological dynamics that influenced their reasoning. The authors suggest that voluntary guidelines, like those proposed by most major medical societies, are inadequate. It may be that only the prohibition of physician-detailer interactions will be effective (Chimonas et al, 2006).

The debate of restriction policies has been newly developed in American medical schools. In recent years the American Medical Student Association established a Pharm Free Campaign to advocate for evidence based, rather than marketing based, prescribing. The study compared the prescription of newly marketed psychotropic medications, none of whom represented a radical breakthrough in their respective classes. It was found that the implementation of a policy to restrict the receipt of gifts from the pharmaceutical industry at US medical schools was associated with significantly reduced prescribing of two out of three newly marketed psychotropic medications among students once they reached clinical practice. The odds of prescribing those new medications were reduced among physicians who graduated from a medical school that had an active gift restriction policy. The propensity to prescribe these two newly introduced medications was further reduced if the students were exposed to the policy for a longer duration or if the policy was relatively stringent. The authors concluded that conflict of interest policies, which have been increasingly adopted by medical schools since 2002, may have the potential to substantially impact clinical practice and

reduce prescribing of newly marketed pharmaceuticals (King et al, 2013).

To overcome some of these barriers and provide correct information on ADs, not biased by economical interests of the pharmaceutical industries, the LHA designed its own drug representative who visited GPs and CMHCs. The LHA drug adviser has perceived a substantial interest on the topic among GPs, who showed to be actively involved (questions, doubts, etc.). Besides, he collected some complaints by GPs, unsatisfied with private clinicians and CMHC psychiatrists sending them patients with already stated prescriptions, not otherwise agreed, or with geriatricians and neurologists prescribing often Duloxetine, either for sub-threshold depression or for any painful condition, etc.

It is noteworthy that a role in facilitating communication was played by the leaflet on antidepressant prescription, created by the LHA audit team to summarize NICE guidelines. It was conceived to be carefully presented by the LHA adviser and was generally appreciated as an interactive communication tool.

## **SWOT Analysis**

With the experience of the failure of the Bolzano project some aspects of the strengths and the weaknesses of this audit became much clearer.

### **Strengths:**

- ◇ Regional Health Government promotes primary care-mental health cooperation
- ◇ Long lasting collaborative experience between PCD and MHD
- ◇ Modern medical records systems
- ◇ Building a consensus on clinical issues
- ◇ Involvement of the Primary Care, the Mental Health Departments, the Pharmaceutical Department and the Clinical Governance Unit in the planning phase of the audit

### **Weaknesses:**

- ◇ Complexity of the process
- ◇ Competing with pharmaceutical
- ◇ Modest economic impact

### **Opportunities:**

- ◇ Better integration between PHC and Mental Health
- ◇ Saving pharmaceutical expenditure and allow good clinical care for all
- ◇ Possible agreements or alliances with other services

### **Threats:**

- ◇ Conflict of interest between marketing and optimal patient care
- ◇ Scepticism toward clinical evidence in scientific literature and guide-lines

At the end of my traineeship it was clear that a project like this is suitable for a very large context, but does not fit to a small reality as Bolzano.

## CONCLUSION

Antidepressant prescriptions have considerably increased all over the world in the last decades. The increasing use of the most expensive agents plays a part in the rising cost of treatments. The Local Health Authority of Bologna has implemented an audit process aimed at improving the appropriateness of outpatient prescriptions focusing on the two branded antidepressants still protected by patent, Escitalopram and Duloxetine.

The Primary Care and the Mental Health Care Departments, as well as the Pharmaceutical Department and the Clinical Governance Unit, were involved in the planning phase of the audit. The audit group, mainly composed of general practitioners and psychiatrists, collected and analyzed scientific evidence on effectiveness and safety of antidepressants. Data on prescriptions of Primary Care Units and Community Mental Health Centers of the Local Health Authority (866.294 inhabitants) were compared, in particular consumption rates of Escitalopram and Duloxetine. The audit group defined the standards to be addressed, the indicators to be evaluated and the actions aimed at reaching the defined goals. NICE guidelines on depression were chosen as reference. The aim of the audit was settled as avoiding Escitalopram and Duloxetine as first choice drugs starting an AD treatment. In order to check the efficacy of the actions undertaken two indicators were selected, consisting in a reduction of 20% of prescriptions of both ADs in outpatient practice and in a 20% reduction of variability across Primary Care Units.

The pre-audit retrospective report (January-April 2012) showed that outpatient antidepressant treatments were prescribed by GPs in over 90% of cases. Audit actions were implemented between November 2012 and May 2013.

Some relevant actions have been integrated with the audit review, such as small-scale educational meetings with GPs and psychiatrists, outreach visits of the LHA prescribing adviser to GPs and CMHCs, leaflets for professionals with information extracted from NICE clinical guidelines, implementation of a web consultation service for GPs about evidence on antidepressants.

Preliminary data have been delivered in August 2013, while the feedback report is expected in November 2013, checking through the selected standards the effectiveness of actions implemented.

It is generally established that clinical audit can be described as a cyclical or spiral systematic process. The spiral suggests that as the process continues, each cycle aspires to a higher level of quality (Benjamin, 2008). Although our preliminary data are partial and do not allow to provide a clear audit feedback up to the present, they first and foremost show that putting the change into practice is possible. However much the close interaction in audit work between GPs and psychiatrists was a powerful facilitating factor, the most important upshot of this process has consisted in further integration between Primary and Mental Health Care.

A SWOT Analysis was carried out to evidence the strengths and weaknesses, opportunities and threats of the process. As identification of weaknesses may be useful to identify relevant strategies

for internal improvement, so the knowledge of threats can amortize factors that may have adverse impacts beyond the control of the Mental Health Department. Better understanding of the strengths and the opportunities facilitates the achievement of the goals set in the project.

## REFERENCES

- Agenzia Italiana del Farmaco. L'uso dei farmaci in Italia – Rapporto OSMed 2011. 2012 Roma: Il Pensiero Scientifico Editore.
- Anderson IM, Ferrier IN, Baldwin RC, Cowen PJ, Howard L, Lewis G, Matthews K, McAllister-Williams RH, Peveler RC, Scott J, Tylee A. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2000 British Association for Psychopharmacology guidelines. *J Psychopharmacol* 2008; 22: 343-96.
- Baker R. Clinical audit in primary health care: towards quality assurance. *BMJ* 1995; 310: 413.1.
- Barbui C, Brambilla P, Campomori A. Antidepressivi SSRI: gli effetti indesiderati più rilevanti. *Informazioni sui Farmaci*. 1999, 1
- Benjamin A. Audit: hot to do it in practice. *BMJ* 2008; 336: 1241-1245
- Best Buy Drugs. The Antidepressants: Treating Depression Comparing Effectiveness, Safety and Price. Consumer Report, 2011.
- Bras PL, Ricordeau P, Roussille B, Saintoyant V. L'information des médecins généralistes sur le médicament. Report No RM 2007-136 P. Inspection générale des affaires sociales. September 2007. Available:<http://lesrapports.ladocumentationfrancaise.fr/BRP/074000703/0000.pdf>. Accessed 10 July 2010.
- Brody H. The Company we keep: Why physicians should refuse to see pharmaceutical representatives. *Ann Fam Med* January 1, 2005; vol. 3 no. 1: 82-85.
- Brunetti M. Meno marketing e più ricerca per una industria in difficoltà. *OdV* 1, 2006. [http://www.odv.bo.it/2006-1//show\\_pdf.php?pdf=editoriale-03.pdf](http://www.odv.bo.it/2006-1//show_pdf.php?pdf=editoriale-03.pdf)
- Cascade E, Kalai AH, Kwentus JA, Bharmal M. Trends in CNS Prescribing Following the Economic Slowdown. *Psychiatry* 2009; 6(1): 15–17.
- Chimonas S, Brennan TA, Rothman DJ. Physicians and drug representatives: exploring the dynamics of the relationship. *J Gen Intern Med* 2007 Feb;22(2):184-90.
- Cipriani A, Barbui C. Sicurezza ed efficacia: il confronto tra i tanti antidepressivi. *Focus Farmacovigilanza* 2009; 56,2.
- Cipriani A, Santilli C, Furukawa TA, Signoretti A, Nakagawa A, McGuire H, Churchill R, Barbui C. Escitalopram versus other antidepressive agents for depression. *Cochrane Database Syst Rev*. 2009.
- Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JP, Churchill R, Watanabe N, Nakagawa A, Ojori IM, McGuire H, Tansella M, Barbui C. Comparative efficacy and acceptability of 12

new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 2009;373(9665): 746-58.

Cipriani A, Koesters M, Furukawa TA, Nosè M, Purgato M, Omori IM, Trespidi C, Barbui C. Duloxetine versus other anti-depressive agents for depression (Review) *Cochrane Database Syst Rev*. 2012

Cosgrove L, Krinsky S. A comparison of DSM-IV and DSM-5 panel members' financial associations with industry: a pernicious problem persists. *PLoS Med* 2012;9:e1001190.

Cruikshank G, MacGillivray S, Bruce D, Mather A, Matthews K, Williams B. Cross-sectional survey of patients in receipt of long-term repeat prescriptions for antidepressant drugs in primary care. *Ment Health Fam Med* 2008; 5: 105-109.

Donabedian A. The quality of medical care. *Science* 1988; 200: 856-964.

Gagnon MA, Lexchin J. The cost of pushing pills: a new estimate of pharmaceutical promotion expenditures in the United States. *PLoS Med* 2008 3 ; 5: e1. doi:10.1371/journal.pmed.0050001.

Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, Mager U, Thieda P, Gaynes BN, Wilkins T, Strobelberger M, Lloyd S, Reichenpfader U, Lohr KN. Comparative benefits and harms of second-generation antidepressants for treating Major Depressive Disorder: an updated meta-analysis. *Annals of Internal Medicine*, 2011; Dec 6;155(11):772-85.

Gartlehner G, Thaler K, Hill S, Hansen RA. How Should Primary Care Doctors Select Which Antidepressants to Administer? *Curr Psychiatry Rep* 2012; 14: 360–369.

Girardi P, Pompili M, Innamorati M, Mancini M, Serafini G, Mazzarini L, Del Casale A, Tatarelli R, Baldessarini RJ. Duloxetine in acute major depression: review of comparisons to placebo and standard antidepressants using dissimilar methods. *Hum. Psychopharmacol Clin Exp*, 2009 Apr; 24(3):177-190.

Granja M. Ligações perigosas. Os Médicos e os Delegados de Informação Médica. *Acta Med Port* 2005; 18: 61-68.

Grassi M. *Occhio Clinico*, 2007, 1: 24-26.

Grol R. Beliefs and evidence in changing clinical practice. *BMJ* 1997, 315: 418-421.

Hong J, Knapp M, McGuire A. Income-related inequalities in the prevalence of depression and suicidal behaviour: a 10-year trend following economic crisis. *World Psychiatry* 2011; 10(1): 40–44.

Insel T. Antidepressants: a complicated picture. <http://www.nimh.nih.gov/about/director>. 2011.



- Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, O'Brien MA, Johansen M, Grimshaw J, Oxman AD. Audit and feedback: effects on professional practice and patient outcomes (Review). *The Cochrane Library* 2012; Issue 7.
- Johnston G, Crombie K, Alder EM, Davies HTO, Millard A. Reviewing audit: barriers and facilitating factors for effective clinical audit. *Quality in Health Care* 2000; 9:23–36.
- King M, Essick C, Bearman P, Ross JS. Medical school gift restriction policies and physician prescribing of newly marketed psychotropic medications: difference-in-differences analysis. *BMJ* 2013 Jan 30;346:f264.
- Lunn MPT, Hughes RAC, Wiffen PJ Duloxetine for treating painful neuropathy or chronic pain (Review) *Cochrane Database Syst Rev*. 2011
- Mazzaglia G. Gli indicatori di appropriatezza come strumento di miglioramento della pratica prescrittiva nella medicina generale. *Care Regioni, Suppl 1*, 2008: 1-4
- Mc Manus P, Mant A, Mitchell PB, Montgomery WS, Marley J, Auland ME. Recent trends in the use of antidepressant drugs in Australia. *Med J Aust* 2000; 173: 458-461.
- Mojtabai R, Olfson M. *Healths Affairs* 2010; 30(8): 1434-1442.
- Moore M, Yuen HM, Dunn N, Mullee MA, Maskell J, Kendrick T. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *BMJ* 2009; 339:b3999.
- National Institute for Health and Clinical Excellence (NICE) Clinical Guidelines 90-91 “Depression. Treatment and management of depression in adults, including adults with a chronic physical health problem”. 2009.
- National Institute for Health and Clinical Excellence (NICE). How to change practice. Understand, identify and overcome barriers to change. 2007
- National Institute for Health and Clinical Excellence (NICE). Principles for Best Practice in Clinical Audit. 2002 Oxford: Radcliffe Medical Press.
- Palmer HR. La valutazione degli interventi sanitari. *Ricerca e Pratica* 1988; 21, 69-126.
- Petty DR, House A, Knapp P, Raynor T, Zermansky A. Prevalence, duration and indications for prescribing of antidepressants in primary care. *Age Ageing* 2006; 35: 523-526.
- Poluzzi E, Piccinni C, Sangiorgi E, Clo M, Tarricone I, Menchetti M, De Ponti F. Trend in SSRI-SNRI antidepressants prescription over a 6-year period and predictors of poor adherence. *Eur J Clin Pharmacol* 2013 ; 10.1007/s00228-013-1567-8

Primary Health Care Clinical Audit Working Group. Clinical audit in primary health care. Department of Health, London:1995.

Qaseem A, Snow V, Denberg TD, Forciea MA, Owens DK. Using Second Generation Antidepressants to Treat Depressive Disorders: a Clinical Practice Guideline from the American College of Physicians. *Annals of Internal Medicine*, 2008.

Reid I. Are antidepressants overprescribed? No. *BMJ* 2013;346:f190

Reid S, Barbui C. Long term treatment of depression with selective serotonin reuptake inhibitors and newer antidepressants. *BMJ* 2010; 340:c1468 doi:10.1136/bmj.c1468

Schueler YB, Koesters M, Wieseler B, Grouven U, Kromp M, Kerekes MF, Kreis J, Kaiser T, Becker T, Weinmann S. A systematic review of duloxetine and venlafaxine in major depression, including unpublished data. *Acta Psychiatr Scand* 2011 Apr; 123(4), 247-265.

Spence D. Are antidepressants overprescribed? Yes. *BMJ* 2013;346:f191

Spurling GK, Mansfield PR, Montgomery BD, Lexchin J, Doust J, et al. (2010) Information from Pharmaceutical Companies and the Quality, Quantity, and Cost of Physicians' Prescribing: A Systematic Review. *PLoS Med* 2010 7(10): e1000352.

Tavazza L. Editoriale. *Quaderni di Sanità pubblica* 1988; Anno 11, novembre, 5-7.

The World Health Organization. The global burden of disease. 2008 Geneva: WHO.

Vuori HV. Optimal and logical quality: two neglected aspects of the quality of health services. *Med Care* 1980; 18: 975-985.

WHO Europe. Social determinants of Health. The solid Facts. 2003.

[http://www.euro.who.int/\\_data/assets/pdf\\_file/0005/98438/e81384.pdf](http://www.euro.who.int/_data/assets/pdf_file/0005/98438/e81384.pdf)